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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/826,629	04/05/2001	Allen David Roses	PU3948US2	3971

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EXAMINER	
CLOW, LORI A	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 03/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/826,629	ROSES, ALLEN DAVID	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1-6 and 8-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election with traverse of Group IV in Paper No. 7 is acknowledged. The traversal is on the grounds that the inventions as claimed can be readily evaluated in one search without placing an undue burden on the Examiner. Applicant's argument is not found persuasive for the reasons set forth in the Restriction/Election Requirement in Paper No. 6, mailed September 25, 2002. In the requirement, specific distinctions between the multiple inventions were set forth and as such the requirement is still deemed proper and is made FINAL.

Claims 1-6 and 8-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 7.

Information Disclosure Statement

Applicant is advised that the IDS filed 1/16/02 was considered and that a copy of PTO-1449 is signed and enclosed.

Claim Rejections - 35 USC § 112

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a method for developing a drug. The claim reads on conducting clinical trials based upon different patient populations and nowhere is there a step or steps that would guide one to develop a drug. Are the claims to a method of drug development

or to a method of clinical trial design? The method steps are inconsistent with the preamble of the claims.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 7 states that patients who have a "like genotype" are to be categorized. However, "like" is an indefinite term. Does this mean that the genotypes are exactly the same or similar? How similar is similar?

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Elston et al. (Statistics in Medicine (1999) Vol. 18:741-751), in view of Kleyn et al. (Science (1998) Vol. 281:1820-1821), in further view of The Nature Biotechnology Roundtable ("Pharmacogenomics:

Revolution or Reaction?" BIO 98' International Meeting and Exposition on June 16, 1998, New York, New York).

Elston et al. disclose a method to study candidate genes in drug trials. The paper specifically discusses the design of a drug trials based upon several considerations. These include genotypes and dosage, the study of more than one gene in one trial, and number of samples in the study. The introduction points to the fact that there have been "several large projects initiated to screen rapidly for polymorphic variants in medically relevant genes and that it is of interest to test whether the polymorphic variants of such candidate genes affect individual response to particular drugs" (page 741). In determining sample size for various trials, Elston et al. explain several statistical methods to achieve the proper outcome. In a multiple test environment, they are able to divide the groups into responders verses non-responders for several iterations (page 744).

Elston et al. do not teach the specific embodiment of making an association between phenotype and genotype. Elston also does not teach conducting subsequent clinical trials on non-responders.

However, Kleyn et al. (Science (1998) Vol. 281 :1820-1821) do propose that there are individual variations in disease expression (phenotype) and drug response (page 1821). In addition, Kleyn et al. review pharmacogenomics and the advances in technology at the time of the invention, putting emphasis on the fact that similar diseases (with obvious distinct clinical symptoms) have distinct etiologies and therefore respond to therapy in very different manners.

Kleyn et al. do not go into specific protocols, such as conducting subsequent clinical trials. However, the Roundtable discussion (BIO 98') presents several critical issues surrounding

the state of clinical trials and drug development. It is certainly suggested that optimally responders and nonresponders would be tested, with the nonresponders being further tested to develop future drugs. On page 18, 1st full paragraph, Daniel Cohen states the following:

"But what is really exciting for pharmaceutical research is the possibility of using clinical trials not only to refine the development of old drugs, but also to discover new targets. Just think about it-some clinical trials involve 5,000 people treated by a given drug. Let's say you have 70% that respond to the drug and 30% that are non-responders. Basically, what you'll do is compare the genotypes of the responders and the nonresponders. You will find genes that predict response, but you will also find genes that predict nonresponse. And those genes predicting nonresponse should show future targets for new drugs that will have no overlap with the first one."

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the various methods of drug trial design with groupings that were centered around patients with like genotypes and different clinical symptoms. In fact it is suggested throughout the review that pharmacogenomics is useful for clinical development of compounds and that variations in disease must be identified.

No claim is allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (703) 306-5439. The examiner can normally be reached on Monday-Friday from 10am to 6:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
GROUP 1800
AU1631

March 5, 2003

Lori A. Clow, Ph.D.
Art Unit 1631

Lori A. Clow